

REVIEW ARTICLE



Efficacy of pharmacological agents for management of post-partum hypertension: A systematic review and network meta-analysis

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Postpartum hypertension is a frequent cause of maternal morbidity and mortality. The objective of this study was to compare the effectiveness and safety of pharmacological agents for management of postpartum hypertension. We searched the MEDLINE and Embase through July 2025. The studies which were randomized controlled trials enrolling women with postpartum hypertension. Eligible trials compared active agents or placebo/usual care and reported blood pressure outcomes. Primary outcomes were time to achieve blood pressure control (hours) and proportion of women achieving blood pressure control within seven days postpartum. Bayesian random-effects network meta-analysis was performed with Metainsight. Thirteen randomized controlled trials were identified. For **time to blood pressure control**, amlodipine and nifedipine ranked highest. Compared with labetalol, amlodipine reduced time to control blood pressure by 5.85 h and nifedipine by 5.11 h. Rankings indicated Calcium Channel Blockers were most effective for rapid control, followed by labetalol. For the **proportion achieving control within seven days**, labetalol ranked highest, with a probability near 100%. Compared with labetalol, risk ratios for blood pressure control were 1.01 for nifedipine, 1.03 for hydralazine, and 1.31 for hydrochlorothiazide–lisinopril. SUCRA values ranked labetalol highest, followed by nifedipine, hydralazine, and hydrochlorothiazide–lisinopril. Calcium channel blockers appear most effective for rapid reduction of blood pressure after childbirth, while labetalol is most reliable for sustained control within the first postpartum week. These findings provide a comparative framework for treatment selection and emphasize the need for larger, rigorously designed postpartum hypertension trials.

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INTRODUCTION

Postpartum hypertension (PPHTN), defined as elevated blood pressure occurring or persisting within six weeks after childbirth, represents a significant cardiovascular complication in the puerperium. Hypertensive disorders of pregnancy (HDP), which include gestational hypertension and preeclampsia, complicate approximately 10% of pregnancies globally and 13–15% in the United States [1, 2]. Recent data indicate an upward trend in HDP-related hospitalizations, rising from 13.3% to 15.9% between 2017 and 2019 [3]. PPHTN encompasses both the persistence of HDP beyond delivery and de novo onset of hypertension in the postpartum period, the latter affecting up to 8% of women within the first week following childbirth [4]. Importantly, nearly 60% of maternal deaths occur within one year postpartum, with HDP being a major contributor [5].

The pathophysiology of PPHTN involves complex transitions in cardiovascular and hormonal systems during the shift from pregnancy to the non-pregnant state, including intravascular volume redistribution and autonomic fluctuations. Women with a history of HDP are at increased risk of chronic hypertension,

coronary artery disease, and stroke, underscoring the need for optimal acute management strategies to improve both short- and long-term outcomes [6]. The condition disproportionately affects certain populations, with the highest prevalence observed among women aged 35–44 years (18.0%) and those identifying as Black (20.9%) or American Indian and Alaska Native (16.4%) [3].

Pharmacological management of PPHTN varies widely across clinical settings. Commonly used antihypertensive agents include labetalol (a combined α - and β -blocker), nifedipine (a calcium channel blocker), hydralazine (a direct vasodilator), and methyldopa (a central α -2 agonist) [7, 8]. Of these, labetalol and methyldopa are often preferred due to their favorable safety profiles in breastfeeding women [9]. While several randomized controlled trials (RCTs) have compared these agents, robust comparative data specific to the postpartum population remain limited. A pivotal trial comparing nifedipine, labetalol, and methyldopa in pregnancy showed all three as effective first-line options [10]. However, systematic reviews have noted that oral labetalol and methyldopa may only be effective in about 50% of pregnant women, emphasizing the need for further evaluation [11].

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Several RCTs have focused specifically on PPHTN, including comparisons between oral nifedipine and oral labetalol. Early network meta-analyses (NMAs) of antihypertensive drugs in pregnancy suggested that nifedipine at various doses was more effective than intravenous labetalol [12–14]. Other NMAs and trial sequential analyses have reported that agents like glyceryl trinitrate and labetalol are associated with fewer maternal adverse effects compared to hydralazine [14]. Nevertheless, the existing evidence is fragmented, with inconsistent methodologies, heterogeneity in outcome definitions, and limited data specific to the postpartum setting.

Given these limitations, clinicians often lack clear, evidence-based guidance on selecting the most appropriate antihypertensive agent in the postpartum period. The postpartum setting introduces unique therapeutic considerations, such as breastfeeding safety, rapid physiological shifts, and the need for prompt blood pressure control. Existing reviews acknowledge the absence of a standardized stepwise pharmacologic strategy for PPHTN [12]. Moreover, treatment decisions can significantly impact maternal outcomes, including hospital readmission rates [15]. Amid increasing emphasis on maternal safety and standardized care pathways, the demand for reliable comparative effectiveness data is urgent.

Therefore, this systematic review and network meta-analysis aim to synthesize the best available evidence from randomized controlled trials to evaluate the comparative effectiveness and safety of antihypertensive agents used in PPHTN. By integrating both direct and indirect comparisons, this analysis seeks to support evidence-based clinical decision-making and improve maternal outcomes during this critical phase of care.

METHODS

Eligibility criteria, information sources and search strategy

This systematic review and network meta-analysis followed the PRISMA extension for Network Meta-Analyses (PRISMA-NMA) reporting guideline [16]. Methodological procedures were guided by the Cochrane Handbook for Systematic Reviews of Interventions, Version 6.4 [17]. MEDLINE and Embase were searched from inception to July 2025, without language restrictions. Reference lists of relevant reviews and eligible articles were screened to identify additional studies. The protocol was prospectively registered with the International Prospective Register of Systematic Reviews (PROSPERO) prior to data collection and analysis. [PROSPERO Registration Number: CRD420251104693] Search strategy and PRISMA check list is available as supplementary file (S1 & S2).

Study selection

Eligible studies were randomized clinical trials (RCTs) enrolling women with **postpartum hypertension** treated with any systemic pharmacological antihypertensive agents. Comparators included other active antihypertensive drugs or placebo/standard care. Trials were required to report at least one prespecified outcome. Nonrandomized studies, antenatal hypertension trials without postpartum data, assessed only non-pharmacological interventions, and those lacking extractable outcome measures were excluded. Two reviewers independently screened all titles, abstracts, and full texts, with disagreements resolved by consensus.

Data extraction and assessment of risk of bias

Three investigators (AS, MPS, RY) independently extracted data on study design, population characteristics, interventions, and outcomes using a standardized form. Risk of bias was assessed with the **Cochrane Risk of Bias 2.0 tool** [18, 19]. Discrepancies were resolved by discussion or by consultation with a third reviewer (SK). The **primary outcomes** were (1) time from delivery to attainment of blood pressure control (measured in hours) and (2) the proportion of women achieving blood pressure control within

seven days postpartum. Definitions for blood pressure control were accepted as per each individual trial, commonly systolic <140 mmHg and diastolic <90 mmHg. The outcomes were finalized by two authors (PT, AS).

Data synthesis

A Bayesian random-effects network meta-analysis was performed by the Meta Insight platform (University of Leicester, UK) which uses gemtc package and network plot was created to show connections among numerous drugs evaluated [20]. Posterior distributions for treatment effect were synthesized by non-informative prior distributions by using Markov Chain Monte Carlo (MCMC) simulations. MCMC convergence has been assessed for each endpoint and presented along with results. Brooks–Gelman diagnostics tool was used to assess convergence. To assess transitivity, the distribution of potential effect modifiers was reviewed across all comparisons. Model convergence was assessed by visual inspection of trace plots and posterior distributions. Consistency between direct and indirect evidence was evaluated using design-by-treatment interaction models and node-splitting approaches [21]. **SUCRA (Surface Under the Cumulative Ranking Curve)** values were also calculated to complement ranking assessments. Treatments were ranked using **cumulative probability**, which represent the mean probability of each intervention being superior to others [22]. For outcomes with ≥ 10 contributing trials, comparison-adjusted funnel plots were constructed to evaluate small-study effects and potential publication bias [23]. Treatment effects were expressed as mean differences (MDs) with 95% confidence intervals (C.I.) for continuous outcomes and risk ratios (RRs) with 95% C.I. for binary outcomes. A two-tailed P value <0.05 was considered statistically significant for all comparisons.

RESULTS

Study selection and characteristics

A total of sixteen RCTs [24–39] were found to be eligible for NMA, out of which three RCTs [27, 31, 35] were excluded due to reporting of either different outcomes or outcomes at different timelines. Eventually, thirteen randomized controlled trials (2005–2025) enrolling a total of 1,625 postpartum women with hypertensive disorders were included for the quantitative analysis (Table 1) (Fig. 1). Studies were conducted in Brazil, India, the United States, Mexico, Pakistan, and Turkey, with sample sizes ranging from 42 to 384 participants.

A wide range of **antihypertensive interventions** were assessed: labetalol, nifedipine (immediate/extended release), amlodipine, enalapril, methyldopa/alpha-methyldopa, hydralazine, clonidine, diltiazem, furosemide (alone or in combination), and hydrochlorothiazide/lisinopril. **Comparators** most frequently included nifedipine, captopril, placebo, amlodipine, labetalol, and enalapril.

Follow-up durations ranged from 24 h (acute BP control studies) to 6 weeks postpartum, with primary outcomes encompassing time to achieve blood pressure (BP) control, proportion of women with BP control at 7 days, need for additional antihypertensives, hospital length of stay, maternal complications (e.g., pulmonary edema, HELLP syndrome, eclampsia), readmission, and breastfeeding-related outcomes.

Two primary evidence networks were formed for the NMA:

1. **Time to achieve BP control (hours):** labetalol, nifedipine, amlodipine, and enalapril.
2. **Proportion achieving BP control within 7 days:** labetalol, nifedipine, hydralazine, and HCTZ/lisinopril combination.

Risk of bias of included studies

Risk of bias was assessed using the **ROB-2 tool** (Fig. 2).

Table 1. Study Characteristics.

Study Authors/Year	Age, mean $\pm$ SD (reported by individual treatment groups)	Sex	Country/Race	Sample size	Intervention (Dose)	Comparator (Dose)	Follow-up duration	Outcomes
Marques R et al. [24]	Methyldopa : 30.0 $\pm$ 7.2 Captopril: 30.4 $\pm$ 7.3	Females	Brazil	172	Captopril: 75 mg/day (25 mg tablet every 8 h).	Methyldopa: 750 mg/day (250 mg tablet every	15 days	Blood pressure control during first 48 h postpartum, blood pressure spike, % requiring treatment Escalation, % requiring treatment de-escalation, Edinburgh Postnatal Depression Scale at Day 15, frequency of side effects
Cursino T et al. [25]	Furosemide: 23.0 $\pm$ 6.9 Placebo: 23.6 $\pm$ 6.3	Females	Brazil	118	Furosemide (40 mg/d orally for 5 days)	Placebo	Length of stay in the hospital	Mean SBP & DBP during hospitalization, frequency of severe hypertensive episodes, Number of antihypertensives at discharge, Time until BP Control, Time from intervention to hospital discharge, Frequency of side effects, frequency of maternal complications.
Pratt K et al. [26]	Amlodipine: 27.9 $\pm$ 6.8 nifedipine ER: 27.8 $\pm$ 5.9	Females	United States of America	175	Amlodipine 2.5 mg/day	Nifedipine ER 30 mg/day	6 weeks	Time from delivery until hospital discharge, acute antihypertensive treatment, discharge dose, need for additional long-acting antihypertensives, side effects, medication discontinuation, breastfeeding outcomes, and readmission rate within 6 weeks postpartum.
Yoselevsky EM et al. [28]	Nifedipine: 33.2 (6.4) Enalapril: 32.4 (6.7)	Females	United States of America	94	Enalapril 10 mg /day	Nifedipine ER 30 mg/day	6 weeks	prolonged hospitalization, unplanned clinic visit, a triage visit, hospital readmission after starting the study agent, time to sustained BP control, need for additional antihypertensives, time to discharge from the hospital, BP at the initial clinic visit after discharge, creatinine levels at follow-up visits, continued need for antihypertensive up to 6 weeks postpartum, side effects, patient reported compliance.
Gupta A et al. [29]	Labetalol: 27.8 $\pm$ 5.4 Amlodipine: 27.4 $\pm$ 5.5	Females	India	130	Labetalol: Oral (100 mg BD)	Amlodipine (2.5 mg BD) Oral	Length of hospital stay	time taken to achieve BP control, dose to achieve control of hypertension, side effects of each drug.

Table 1. continued

Study Authors/Year	Age, mean $\pm$ SD (reported by individual treatment groups)	Sex	Country/Race	Sample size	Intervention (Dose)	Comparator (Dose)	Follow-up duration	Outcomes
Bartal MF et al. [30]	combined hydrochlorothiazide and lisinopril : 30.0 (28.03 $\pm$ 3.5) Nifedipine: 33.00 (27.03 $\pm$ 6.3)	Females	United States of America	67	Combined hydrochlorothiazide (12.5 mg/day) and lisinopril (10 mg/day)	Nifedipine(30 mg/day)	6 weeks	average BP over days 7 to 10 after delivery, severe maternal morbidity up to 6 weeks after delivery, severe BP requiring intravenous medications, post-partum hospital length of stay, sBP and dBP during the first clinic visit, medication compliance at 7 to 10 days after delivery and during the postpartum period, and adverse events.
Perdigao JL et al. [32]	Furosemide: 27 (22–32) Placebo : 27 (23–33)	Females	United States of America	384	Furosemide 20 mg oral	Placebo	6 weeks	prevalence of persistent hypertension 7-days postpartum, days required to achieve resolution of hypertension,% of postpartum severe BP, need for additional antihypertensive medications postpartum, postpartum readmissions or emergency visits, postpartum length of stay, pulmonary edema and severe maternal morbidity, adverse effects, neonatal ICU admission, self-reported breastfeeding issues
Arias-Hernandez et al. [33]	Diltiazem: 21.6 (6.8) Nifedipine: 23.2 (6.2)	Females	Mexico	42	Diltiazem (60 mg) TDS	Nifedipine (10 mg) TDS	48 h	SBP, DBP and HR, number of hypertension and hypo-tension episodes and ICU length of stay.
Ainuddin J et al. [34]	Labetalol: 26.7 $\pm$ 1.9 Nifedipine: 25.9 $\pm$ 1.8	Females	Pakistan	124	Labetalol 100 mg QID	Nifedipine LA 30 mg/day	72 h	time to achieve BP control, sustained BP control, need of additional antihypertensive medications, length of hospital stay, drug related side effects.
Sharma KU et al. [36]	Labetalol : 34.0 (7.4) Nifedipine ER: 33.3 (6.4)	Females	United States of America	50	Labetalol 200 mg PO BID escalating to 800 mg PO BID	Nifedipine ER 30 mg PO daily escalating to 90 mg PO daily	6 weeks	time to achieve BP control, postpartum length of stay, the need for increased dosing, need for additional IV and oral antihypertensive medication, side effects

Table 1. continued

Study Authors/Year	Age, mean $\pm$ SD (reported by individual treatment groups)	Sex	Country/Race	Sample size	Intervention (Dose)	Comparator (Dose)	Follow-up duration	Outcomes
Noronha Neto C et al [37]	Clonidine: 28.9 (6.7) Captopril: 28.8 (6.7)	Females	Brazil	88	Active 1: oral clonidine (0.1 mg) Active 2: oral captopril (2.5 mg)	-----	Length of hospital stay	frequency of very high BP episodes; daily mean SBP and DBP levels; number of days with very high BP episodes; number of days until BP was controlled; percentage reduction in SBP; % reduction in DBP; number of doses used to control BP; need to add another hypertensive agent; number of antihypertensives added; need for sodium nitroprusside; maternal complications; adverse effects; number of days in obstetric ICU and death.
Vigil-De Gracia et al. [38]	Hydralazine: 29.9 $\pm$ 5.9 Labetalol: 31.3 $\pm$ 5.5	Females	United States of America	82	Hydralazine (5 mg slow bolus given intravenously, and repeated every 20 min to a maximum of 5 doses)	labetalol (20 mg intravenous bolus dose followed by 40 mg if not effective within 20 min, followed by 80 mg every 20 min to a maximum dose of 300 mg)	24 h	lowering of BP, uncontrolled BP, need for additional antihypertensive therapy, doses of antihypertensive, eclampsia, HELLP syndrome, pulmonary edema, oliguria, DIC, hypertensive encephalopathy, maternal heart rate $\geq$ 100 beats/min, maternal side-effects
Sayin N et al. [39]	Alpha-methyldopa: 28.1 $\pm$ 5.9 Nifedipine: 27.1 $\pm$ 5.9	Females	Turkey	83	Alpha-methyldopa (750 mg/d)	Nifedipine (40 mg/d)	Time taken to achieve normotension	Monotherapy success rates, dual or triple therapy required, lab parameters, Medication needed after 7 days.

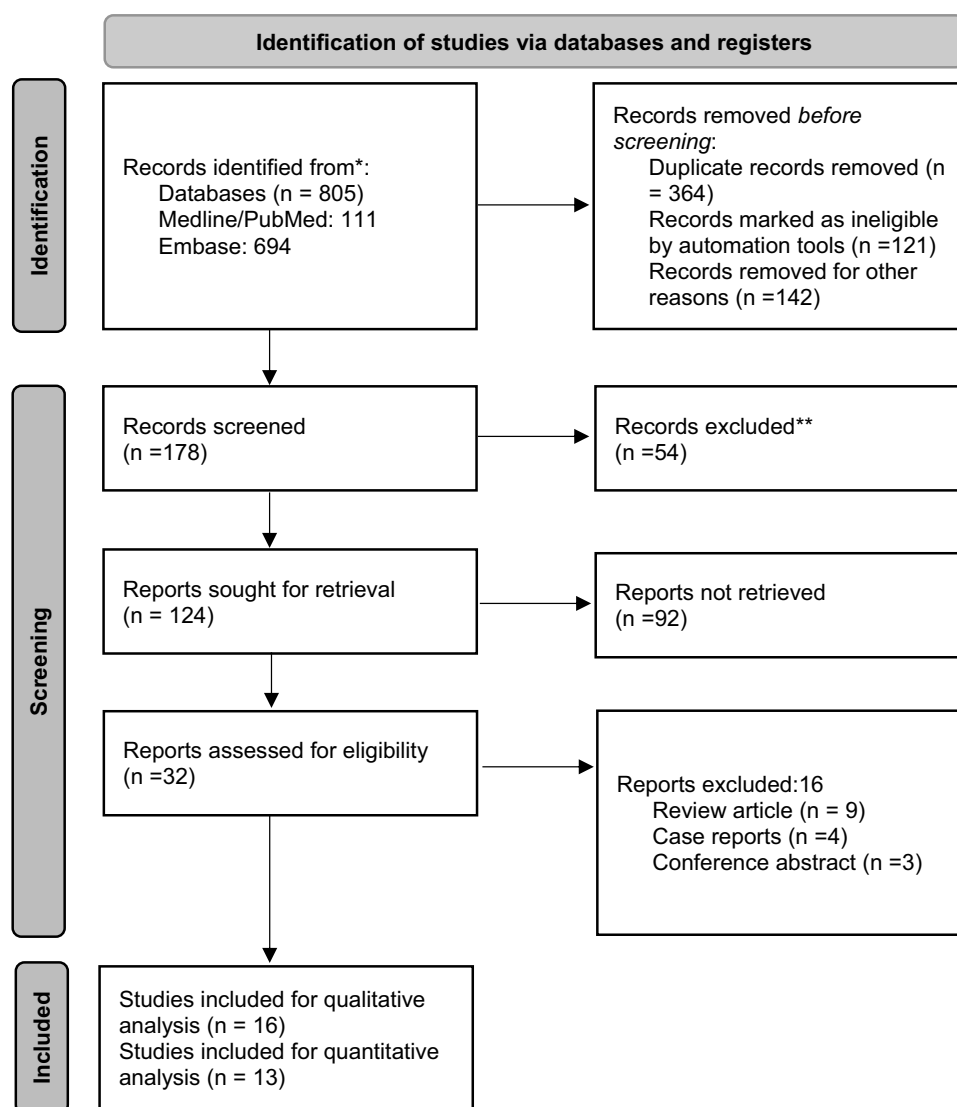


Fig. 1 PRISMA Flow Chart. *Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers). **If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools. Source: Page MJ, et al. BMJ 2021;372:n71. <https://doi.org/10.1136/bmj.n71>. This work is licensed under CC BY 4.0. To view a copy of this license, visit <https://creativecommons.org/licenses/by/4.0/>.

- **Low risk or some concerns:** Several trials (e.g., Gupta 2023, Sharma 2017, Perdigao 2021, Pratt 2025, Cursino 2025, Vigil-de Gracia 2007, Noronha 2017) demonstrated relatively low bias, with minor issues mainly in deviations from interventions.
- **High risk:** Other trials (e.g., Ainuddin 2019, Bartal 2023, Marques 2025, Sayin 2005, Hernandez 2020, Yoselevsky 2023) were judged high risk, primarily due to unclear or inadequate randomisation processes and missing outcome data.
- **Domains most affected:** Randomisation (D1) and missing data (D3) were the most frequent sources of high risk. Outcome measurement (D4) and selective reporting (D5) were generally low risk.

Overall, the evidence base consists of a mix of rigorously conducted recent RCTs and older or smaller studies with methodological limitations, necessitating cautious interpretation of treatment rankings. Node-splitting and consistency checks indicated no significant disagreement between direct and indirect evidence ($p > 0.05$), supporting the use of the consistency model.

Synthesis of results

Time to achieve blood pressure control. A total of four anti-hypertensive agents—**labetalol, nifedipine, amlodipine, and enalapril**—were evaluated across the included randomized controlled trials for the outcome of time (in hours) to achieve postpartum blood pressure control. Labetalol was the most frequently studied agent and served as the reference for analysis.

MCMC convergence assessment: The Bayesian random-effects network meta-analysis demonstrated robust convergence across all parameters. Convergence diagnostics showed excellent performance: shrink factors (R-hat) approached 1.0 (< 1.05) by approximately 5,000 iterations for all treatment comparisons (d.Nifedipine.Amlodipine, d.Nifedipine.Enalapril, d.Nifedipine.Labetalol) and the between-study heterogeneity parameter (sd.d). Trace plots confirmed good chain mixing and stationarity across all four MCMC chains (20,000 iterations each after 5,000 burn-in iterations, number of chains 4), ensuring reliable posterior estimates.

Unique ID	Study ID	Experimental	Comparator	D1	D2	D3	D4	D5	Overall	
1	Gupta A 2023	Labetalol	Amlodipine	+	!	+	+	+	!	+
2	Sharma KJs 2017	Labetalol	Nifedipine	+	!	+	+	+	!	+
3	Ainuddin 2019	Labetalol	Nifedipine	+	!	+	+	+	!	+
4	Bartal MF 2023	Hydrochlorothiazide/Lisinopril	Nifedipine	+	!	+	+	+	!	+
5	Perdiago JL 2021	Furosemide	Placebo	+	!	+	+	+	!	+
6	Pratt K 2025	Amlodipine	Nifedipine	+	!	+	+	+	!	+
7	Marques R 2025	Methyldopa	Captopril	+	!	!	+	+	!	+
8	Sayin N 2005	Alpha-methyldopa	Nifedipine	+	!	+	+	+	!	+
9	Hernandez A 2020	Diltiazem	Nifedipine	+	!	+	+	+	!	+
10	Yoselevsky EM 2023	Nifedipine	Enalapril	+	!	+	+	+	!	+
11	Cursino T 2025	Furosemide	Placebo	+	!	+	+	+	!	+
12	Vigil de gracia 2007	Hydralazine	Labetalol	+	!	+	+	+	!	+
13	Noronha N 2017	Clonidine	Captopril	+	!	+	+	+	!	+

+ Low risk
 ! Some concerns
 - High risk

D1 Randomisation process
 D2 Deviations from the intended interventions
 D3 Missing outcome data
 D4 Measurement of the outcome
 D5 Selection of the reported result

Fig. 2 Risk of Bias Assessment.

Pairwise and network meta-analysis: The **Bayesian random-effects network meta-analysis with confirmed convergence** revealed that, compared with labetalol (reference):

- **Amlodipine:** MD – 5.85 h (95% C.I.: –21.3, 11.4) - associated with shorter time to BP control
- **Nifedipine:** MD – 5.11 h (95% C.I.: –17.9, 9.71) - associated with shorter time to BP control
- **Enalapril:** MD + 23.7 h (95% C.I.: –9.25, 57.3) - associated with longer time to BP control

All pairwise comparisons: The comprehensive treatment comparison matrix revealed:

- **Amlodipine vs. Nifedipine:** MD 0.84 h (95% C.I.: –15.9, 17.6) - minimal difference
- **Enalapril vs. Amlodipine:** MD 29.3 h (95% C.I.: –5.13, 63.7) - enalapril slower
- **Enalapril vs. Nifedipine:** MD 28.6 h (95% C.I.: –2.31, 59.3) - enalapril slower

Treatment ranking (Fig. 3A–C): **Surface Under the Cumulative Ranking (SUCRA) analysis** indicated a clear hierarchy for speed of BP control:

1. **Amlodipine** (SUCRA = 79.7%): Most likely to achieve fastest BP control
2. **Nifedipine** (SUCRA = 75.2%): Second most effective for rapid BP control
3. **Labetalol** (SUCRA = 40.3%): Intermediate effectiveness
4. **Enalapril** (SUCRA = 4.8%): Slowest to achieve BP control

Consistency assessment (supplementary file S3): Node-splitting analysis and consistency plots showed good agreement between direct and indirect evidence across all comparisons (p-values > 0.05), supporting the validity of the consistency model assumptions.

Proportion of women achieving blood pressure control within seven days postpartum. A total of four antihypertensive agents—**labetalol, nifedipine, hydralazine, and HCTZ/lisinopril combination**—were evaluated across the included randomized controlled trials for the binary outcome of achieving postpartum blood pressure control within seven days. Based on the network structure, labetalol served as the reference treatment for the analysis.

MCMC convergence assessment: The Bayesian random-effects network meta-analysis demonstrated robust convergence across all parameters. Convergence diagnostics showed excellent performance: shrink factors (R-hat) approached 1.0 (< 1.05) by approximately 5000 iterations for all treatment comparisons

(d.Labetalol.Hydralazine, d.Labetalol.Nifedipine, d.Labetalol.HCTZ_Lisinopril) and the between-study heterogeneity parameter (sd.d). Trace plots confirmed good chain mixing and stationarity across all four MCMC chains (20,000 iterations each after 5,000 burn-in iterations, chain 04), ensuring reliable posterior estimates. (supplementary file S4).

Pairwise and network meta-analysis: The Bayesian random-effects network meta-analysis with confirmed convergence revealed that compared with labetalol (reference), all alternative treatments showed numerically higher risk ratios, indicating potentially lower effectiveness:

- **HCTZ/Lisinopril combination:** RR 1.31 (95% C.I.: 0.460, 3.49)
- **Hydralazine:** RR 1.03 (95% C.I.: 0.494, 2.16)
- **Nifedipine:** RR 1.01 (95% C.I.: 0.547, 1.75)

All pairwise comparisons: The comprehensive treatment comparison matrix revealed that:

- **Nifedipine vs. Hydralazine:** RR 0.99 (95% C.I.: 0.57, 1.83)
- **HCTZ/Lisinopril vs. Hydralazine:** RR 1.28 (95% C.I.: 0.35, 4.32)
- **HCTZ/Lisinopril vs. Nifedipine:** RR 1.29 (95% C.I.: 0.56, 2.99)

Treatment ranking (Fig. 4A–C): **Surface Under the Cumulative Ranking (SUCRA) analysis** indicated a clear hierarchy in the probability of achieving blood pressure control within seven days:

1. **Labetalol** (SUCRA ≈ 100%): Consistently ranked as the most effective treatment
2. **Nifedipine** (SUCRA ≈ 60%): Second most likely to achieve BP control
3. **Hydralazine** (SUCRA ≈ 35%): Intermediate effectiveness
4. **HCTZ/Lisinopril** (SUCRA ≈ 5%): Lowest probability of achieving BP control within seven days

Since both outcomes included fewer than 10 studies, assessment of publication bias was not feasible.

Overall evidence synthesis and implications

Taken together, the evidence suggests that amlodipine and nifedipine are most promising for rapid BP control, whereas labetalol is the most reliable for sustained control within seven days. Enalapril and HCTZ/lisinopril combinations appear less effective. Although confidence intervals remain wide due to the limited sample sizes and number of trials, the convergence diagnostics, low-to-moderate heterogeneity, and network consistency support the robustness of these findings. Importantly, these results should be interpreted as probabilistic rankings rather than definitive treatment effects, and they highlight the urgent need for larger, rigorously designed postpartum hypertension trials to establish a clear treatment hierarchy.

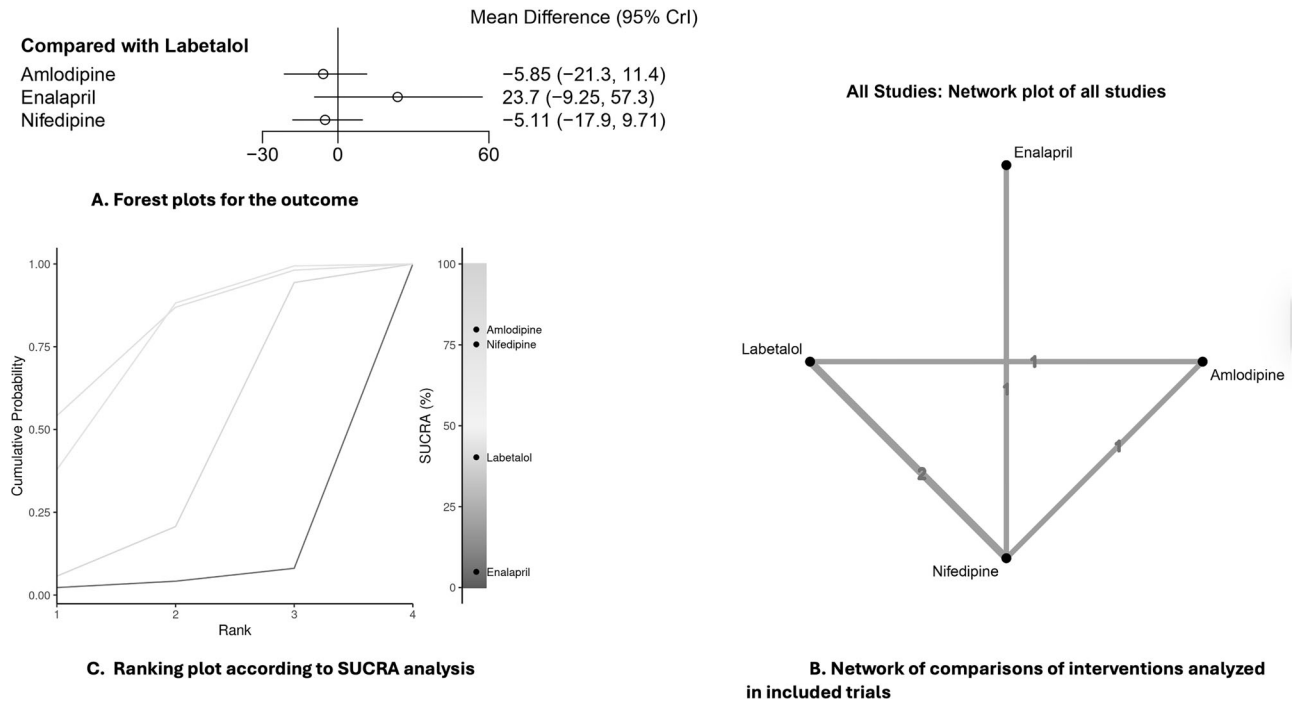


Fig. 3 Ranking for different drugs for the outcome i.e., Time to achieve BP control (in hours). **A.** Forest plots for the outcome **B.** Network of comparisons of interventions analyzed in included trials **C.** Ranking plots according to SUCRA analysis.

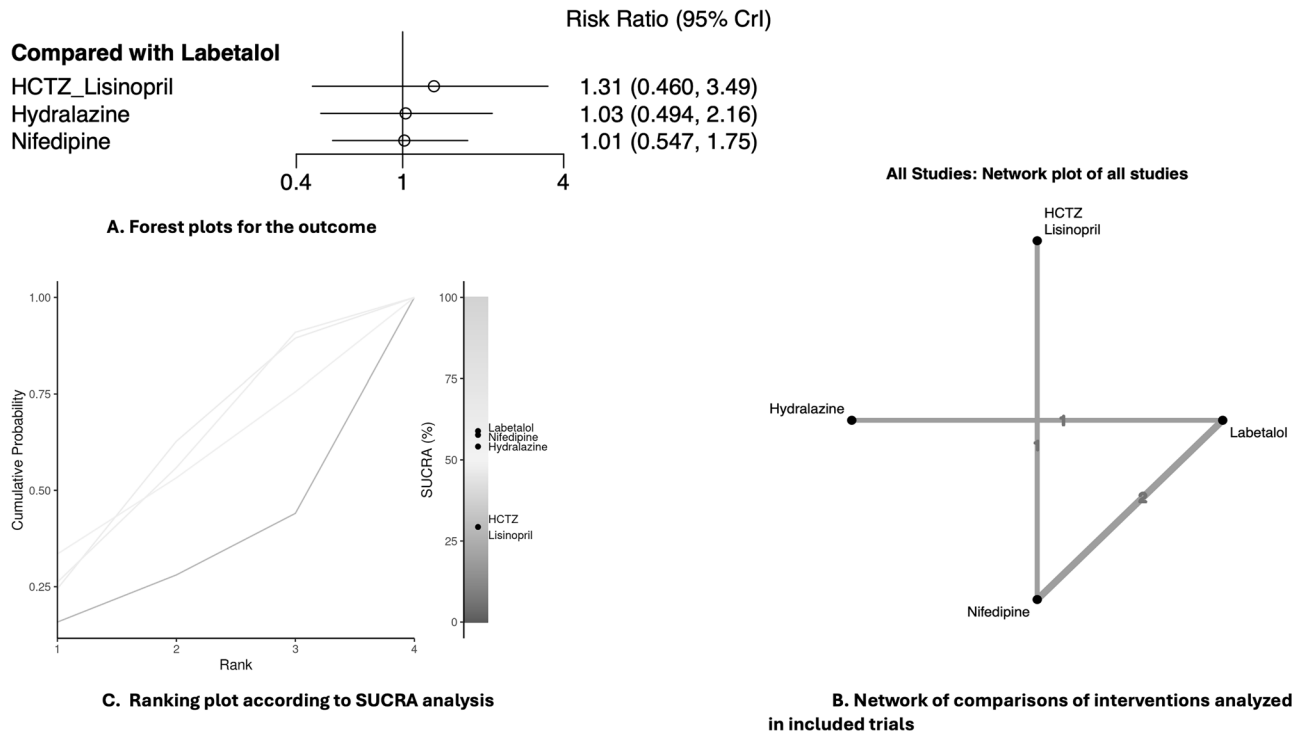


Fig. 4 Ranking for different drugs for the outcome i.e., Proportion achieving BP control within 7 days. **A.** Forest plots for the outcome **B.** Network of comparisons of interventions analyzed in included trials **C.** Ranking plots according to SUCRA analysis.

DISCUSSION

In this network meta-analysis of randomized controlled trials evaluating pharmacological management of postpartum hypertension, we identified clinically meaningful differences in treatment performance depending on the outcome of interest. For rapid blood pressure control, calcium channel blockers (CCBs)—

particularly amlodipine and nifedipine—ranked highest, achieving blood pressure reduction approximately 5–6 h earlier than labetalol. This finding is consistent with the HIPPO randomized controlled trial, which demonstrated that amlodipine achieved sustained blood pressure control a mean of 7.2 h earlier than oral labetalol in postpartum women with hypertension [29]. Similarly, a

trial comparing extended-release nifedipine with oral labetalol reported shorter time to achieve BP targets with nifedipine (≈ 30.4 h vs. 35.6 h) [36].

Mechanistically, these observations are biologically plausible. CCBs act directly on vascular smooth muscle, blocking L-type calcium channels to produce rapid vasodilation and an immediate fall in systemic vascular resistance. This explains their superior performance in acute stabilization and the faster speed of BP recovery noted in both our network analysis and individual RCTs [10]. In contrast, enalapril—a prototypical angiotensin-converting enzyme (ACE) inhibitor—exerts its antihypertensive effect by suppressing the renin–angiotensin–aldosterone system, reducing angiotensin II and aldosterone, and promoting gradual vascular remodeling. This indirect mechanism results in slower onset of BP reduction. The PICK-UP feasibility trial demonstrated that enalapril improved postnatal cardiac structure and diastolic function after preterm preeclampsia, highlighting benefits for medium- to long-term cardiovascular outcomes rather than immediate postpartum BP lowering [40].

For the proportion of women achieving blood pressure control within seven days postpartum, our analysis ranked labetalol as the most effective treatment, with nifedipine and hydralazine showing intermediate performance. This aligns with previous clinical observations where labetalol, due to its combined α - and β -adrenergic blockade, provides steady control without large fluctuations in hemodynamics [41]. By contrast, ACE inhibitor-based regimens such as hydrochlorothiazide–lisinopril combinations were consistently less effective in short-term postpartum BP control, reinforcing their limited role in the immediate postpartum setting.

Our findings are in agreement with recent comparative effectiveness studies. A multicenter non-inferiority RCT reported that amlodipine was comparable to nifedipine extended-release in postpartum hypertension, though differences emerged in tolerability and discontinuation rates [26]. Observational studies further suggest that nifedipine may be associated with fewer readmissions for hypertensive complications compared with labetalol, particularly in North American cohorts [42–45]. Together with our NMA, these results support the preferential use of CCBs for rapid stabilization, while reserving labetalol for reliable longer-term control across the first postpartum week. Despite consistent trends, caution is warranted in interpretation. Many trials were underpowered, varied in their definitions of blood pressure control, and used heterogeneous dosing regimens. Moreover, few studies assessed maternal and neonatal safety in a standardized fashion, limiting firm conclusions regarding comparative safety. Enalapril, for example, is considered safe during lactation, with minimal drug transfer into breast milk, yet its slow onset diminishes its utility for urgent postpartum hypertension control.

These findings are further contextualized by recent systematic reviews and contemporary guidance on postpartum hypertension management. Evidence syntheses have consistently highlighted substantial heterogeneity in postpartum antihypertensive practices, including variability in treatment thresholds, agent selection, dosing strategies, and follow-up duration, reflecting persistent gaps in high-quality, standardized evidence for this critical period and lack of high quality studies [46, 47]. Emerging data suggest that women with more severe antepartum disease or early postpartum blood pressure elevations are more likely to require antihypertensive up-titration, underscoring the need for early risk stratification and close monitoring in the immediate postpartum phase [48]. Contemporary cardiovascular reviews emphasize the adequate management of postpartum hypertension not only for preventing acute complications but also for mitigating long-term cardiovascular risk, reinforcing the importance of timely and effective blood pressure control strategies tailored to short- and medium-term goals [5]. Importantly, current guideline-based reviews indicate calcium channel blockers and beta blockers to

be the drug of choice for control of blood pressure during breastfeeding, allowing clinicians to balance maternal blood pressure control with neonatal safety [49]. These findings also support our results about use of calcium channel blockers and beta blockers for postpartum hypertension. Taken together, these data reinforce the clinical relevance of our network meta-analysis and support a differentiated, goal-directed approach to postpartum hypertension management, as suggested by our findings.

Clinical implications

Our findings suggest a goal-directed therapeutic strategy:

- **For rapid stabilization**, CCBs such as nifedipine or amlodipine are most effective.
- **For steady, reliable control over the first week**, labetalol may be more appropriate.
- **ACE inhibitors (e.g., enalapril) and ACE inhibitor–diuretic combinations** may have a role in longer-term cardiovascular remodelling but are less effective for immediate postpartum BP reduction. Moreover, limited data on ACE inhibitors and reduced milk production with diuretics supports caution about their use (5,48).

The evidence base remains limited, with wide credible intervals reflecting small sample sizes and heterogeneous designs. Larger, multicentre RCTs with harmonized BP endpoints and standardized safety reporting are urgently needed to confirm treatment hierarchies, evaluate combination therapies, and clarify maternal and neonatal safety profiles across diverse populations. This network meta-analysis provides a comprehensive synthesis of pharmacologic strategies for postpartum hypertension. CCBs appear most effective for rapid BP control due to their direct vasodilatory action, labetalol is superior for sustained control, and enalapril may be best suited for longer-term cardiovascular remodelling rather than acute stabilization. Until adequately powered trials are available, clinical decision-making should remain individualized, balancing pharmacologic properties, therapeutic goals, breastfeeding considerations, and local availability. To the best of our knowledge it's the first network meta-analysis for postpartum hypertension. The inclusion of studies from different countries makes it meaningful, however as per our assessment less number of studies (13) and five studies were at high risk of bias which dents the ultimate results. Authors were not able to perform certainty of evidence analysis due to partially disconnected networks.

CONCLUSION

In this first network meta-analysis of pharmacological treatments for postpartum hypertension, calcium channel blockers (amlodipine and nifedipine) ranked highest for rapid blood pressure reduction, whereas labetalol was most effective for sustained control within seven days. Enalapril and hydrochlorothiazide–lisinopril combinations consistently ranked lowest across outcomes. Although these findings provide a comparative framework for treatment selection, wide credible intervals and variable study quality underscore the need for larger, rigorously conducted randomized trials. Together, the results suggest that treatment choice may be guided by the clinical objective—rapid stabilization or sustained control—while further research is needed to confirm these hierarchies and strengthen the evidence base for postpartum hypertension management.

What is already known

- Commonly used drugs for postpartum hypertension include **labetalol, nifedipine, amlodipine, methyldopa, hydralazine**, and occasionally **diuretics** such as **hydrochlorothiazide**. Their use is largely extrapolated from pregnancy or

general hypertension data, with limited comparative evidence in the postpartum setting.

What this study adds

- This study provides the **first network meta-analysis** ranking drug efficacy in postpartum hypertension: **Amlodipine** and **nifedipine** are most effective for **rapid BP reduction**, followed by **labetalol**, which offers the most **sustained control** within the first week. **Hydralazine** and **hydrochlorothiazide-lisinopril** showed lower probability of achieving early control. In addition, converting enzyme inhibitors and angiotensin II receptor blockers should be used with caution due to limited evidence.

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AUTHOR CONTRIBUTIONS

AS and PT conceptualized the analysis. AS, MPS, and RY extracted the data including data search. AS, MPS, SUK, drafted the manuscript. All authors approved the manuscript.

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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